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Just

Folic acid [59-30-3]

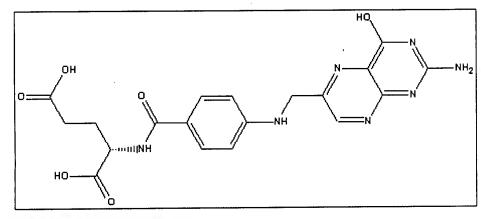
Synonyms: Vitamin M; Pteroylglutamic Acid; folacin; folcysteine;

N-(p-(((2-amino-4-hydroxy-6-pteridinyl)methyl)amino)benzoyl)-L-glutamic acid;

N-(4-(((2-amino-1,4-dihydro-4-oxo-6-pteridinyl)methyl)amino)benzoyl)-L-glutamic acid;

L-pteroylglutamic acid; pteglu;

2-amino-6-((p-((1,3-dicarboxypropyl)carbamoyl)anilino)methyl)-4-pteridinol; pteroyl-L-glutamic acid; pteroylmonoglutamic acid; pteroyl-L-monoglutamic acid; Vitamin B11; Vitamin BC; PGA; liver lactobacillus casei factor; cytofol; foliamin; folipac; folsaure; foluite; incafolic; millafol; folettes; acifolic; folsav; folacid; Vitamin B; folbal;



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VIEW CHEM3D MODEL

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FILE 'REGISTRY' ENTERED AT 13:05:55 ON 07 NOV 2000
=> s c20h25n7o6
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L1
=> s 5-methyl/cns
       3229144 5/CNS
       4703475 METHYL/CNS
L2
        281164 5-METHYL/CNS
                  ((5(W)METHYL)/CNS)
\Rightarrow s 11 and 12
            44 L1 AND L2
L3
=> s 2-amino/cns and 4-hydroxy/cns
       8430573 2/CNS
       1895456 AMINO/CNS
        181444 2-AMINO/CNS
                  ((2(W)AMINO)/CNS)
       6216541 4/CNS
       1330512 HYDROXY/CNS
        225667 4-HYDROXY/CNS
                  ((4(W)HYDROXY)/CNS)
L4
          2657 2-AMINO/CNS AND 4-HYDROXY/CNS
=> s 14 and 13
            11 L4 AND L3
L5
=> s
     L-Glutamic acid/cns
        868829 L/CNS
         39551 GLUTAMIC/CNS
       4709356 ACID/CNS
L6
         31484 L-GLUTAMIC ACID/CNS
                  ((L(W)GLUTAMIC(W)ACID)/CNS)
\Rightarrow s 2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pterid?/cns
       8430573 2/CNS
       1895456 AMINO/CNS
          4422 1,4,5,6,7,8/CNS
        317083 HEXAHYDRO/CNS
       3229144 5/CNS
       4703475 METHYL/CNS
       6216541 4/CNS
       1462899 OXO/CNS
       2176424 6/CNS
         19070 PTERID?/CNS
L7
            86 2-AMINO-1, 4, 5, 6, 7, 8-HEXAHYDRO-5-METHYL-4-OXO-6-PTERID?/CNS
((2(W)AMINO(W)1,4,5,6,7,8(W)HEXAHYDRO(W)5(W)METHYL(W)4(W)OXO(W
                 )6(W)PTERID?)/CNS)
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=> s 16 and 17

 \Rightarrow s 18 and 7/n

166612 7/N 44 L8 AND 7/N L9

=> d scan

ь9 44 ANSWERS REGISTRY COPYRIGHT 2000 ACS

IN L-Glutamic acid, N-[4-[[(2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-, compd. with 1-ethyl-2pyrrolidinemethanamine (1:1) (9CI) C20 H25 N7 O6 . C7 H16 N2

MF

CM 1

CM 2

IN L-Glutamic acid, N-[4-[[(2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl)methyl]amino]-2-iodobenzoyl]- (9CI)

MF C20 H24 I N7 O6

Absolute stereochemistry.

L9 44 ANSWERS REGISTRY COPYRIGHT 2000 ACS

IN L-Glutamic acid, N-[4-[[(2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl)methyl-t]amino]benzoyl-3,5-t2]- (9CI)

MF C20 H22 N7 O6 T3

IN L-Glutamic acid, N-[4-[[(2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-, monopotassium salt (9CI)

MF C20 H25 N7 O6 . K

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L9 44 ANSWERS REGISTRY COPYRIGHT 2000 ACS

IN L-Glutamic acid, N-[4-[[(2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-, (R)-, compd. with cyclohexanamine (9CI)

MF C20 H25 N7 O6 . x C6 H13 N

CM 1

CM 2

L9 44 ANSWERS REGISTRY COPYRIGHT 2000 ACS

IN L-Glutamic acid, N-[4-[[(2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-, labeled with tritium (9CI)

MF C20 H25 N7 06

IN L-Glutamic acid, N-[4-[[(2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-, ion(2-) (9CI)

MF C20 H23 N7 O6

Absolute stereochemistry.

L9 44 ANSWERS REGISTRY COPYRIGHT 2000 ACS

IN L-Glutamic acid, N-[4-[[(2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-, compd. with 2-aminoethanol (9CI)

MF C20 H25 N7 O6 . x C2 H7 N O

CM 1

$$\begin{smallmatrix} H&_2&N& & C&H&_2& & C&H&_2& & \\ \end{smallmatrix}$$

2 CM

Absolute stereochemistry.

L9 44 ANSWERS REGISTRY COPYRIGHT 2000 ACS

Magnesium, [N-[4-[[(2-amino-3,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-IN pteridinyl)methyl]amino]benzoyl]-L-glutamato(2-)]- (9CI)

C20 H23 Mg N7 O6 CCS, COM MF

CI

IN L-Glutamic acid, N-[4-[[(2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-, compd. with L-arginine (1:2) (9CI)

MF C20 H25 N7 O6 . 2 C6 H14 N4 O2

CM 1

Absolute stereochemistry.

CM 2

Absolute stereochemistry.

L9 44 ANSWERS REGISTRY COPYRIGHT 2000 ACS

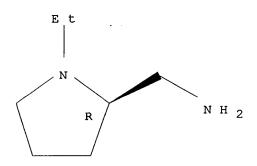
IN L-Glutamic acid, N-[4-[[(2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-, (S)-, compd. with (R)-1-ethyl-2-pyrrolidinemethanamine (1:1) (9CI)

MF C20 H25 N7 O6 . C7 H16 N2

CM 1

CM 2

Absolute stereochemistry.



L9 44 ANSWERS REGISTRY COPYRIGHT 2000 ACS

IN L-Glutamic acid, N-[4-[[2-(2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl)ethyl]amino]benzoyl]-, bis(phenylmethyl) ester (9CI)

MF C35 H39 N7 O6

IN L-Glutamic acid, N-[4-[[2-(2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl)ethyl]amino]benzoyl]-, disodium salt (9CI)

MF C21 H27 N7 O6 . 2 Na

Absolute stereochemistry.

2 Na

IN L-Glutamic acid, N-[4-[[[(6S)-2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl]methyl]amino]benzoyl]-, sodium salt (9CI)
MF C20 H25 N7 O6 . x Na

Absolute stereochemistry.

• x Na

L9 44 ANSWERS REGISTRY COPYRIGHT 2000 ACS

IN L-Glutamic acid, N-[4-[[(2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-, calcium salt, (R)- (9CI)
MF C20 H25 N7 O6 . x Ca

Са

REGISTRY COPYRIGHT 2000 ACS L9

L-Glutamic acid, N-[4-[[(2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl)methyl]methylamino]benzoyl]-, calcium salt (1:1) (9CI) C21 H27 N7 O6 . Ca IN MF

● Ca

L9 44 ANSWERS REGISTRY COPYRIGHT 2000 ACS

IN L-Glutamic acid, N-[4-[[(2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-, calcium salt (1:1) (9CI)

MF C20 H25 N7 O6 . Ca

Са

L9 44 ANSWERS REGISTRY COPYRIGHT 2000 ACS

IN 6-pteridinyl)methyl]amino]benzoyl]-, (R)-, compd. with .gamma.-cyclodextrin (1:1) (9CI)
C48 H80 O40 . C20 H25 N7 O6

MF

1 CM

CM 2

•

IN L-Glutamic acid, N-[4-[[2-(2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl)ethyl]amino]benzoyl]-, (R)- (9CI)

MF C21 H27 N7 O6

IN L-Glutamic acid, N-[4-[[(2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-, sodium salt (9CI)

MF C20 H25 N7 O6 . x Na

IN L-Glutamic acid, N-[4-[[(2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-, magnesium salt (1:1) (9CI)

MF C20 H25 N7 O6 . Mg

Absolute stereochemistry.

Mg

L9 44 ANSWERS REGISTRY COPYRIGHT 2000 ACS

IN L-Glutamic acid, N-[4-[[(2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-, compd. with cyclohexanamine (9CI) MF C20 H25 N7 O6 . x C6 H13 N

CM 1

CM2

L9 44 ANSWERS REGISTRY COPYRIGHT 2000 ACS

L-Glutamic acid, N-[4-[[(2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl)methyl]formylamino]benzoyl]- (9CI) C21 H25 N7 O7 IN

MF

IN L-Glutamic acid, N-[4-[[(2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl)methyl]methylamino]benzoyl]- (9CI)

MF C21 H27 N7 O6

CI COM

Absolute stereochemistry.

L9 44 ANSWERS REGISTRY COPYRIGHT 2000 ACS

IN L-Glutamic acid, N-[4-[[(2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-, (S)-, compd. with N-(1-methylethyl)-2-propanamine (9CI)

MF C20 H25 N7 O6 . x C6 H15 N

Absolute stereochemistry.

CM 2

- L9 44 ANSWERS REGISTRY COPYRIGHT 2000 ACS
- IN L-Glutamic acid, N-[4-[[(2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-, dibutyl ester (9CI)
 MF C28 H41 N7 O6

IN L-Glutamic acid, N-[4-[[[(68)-2-amino-1,4,5,6,7,8-hexahydro-5-methyl-

4-oxo-6-pteridinyl]methyl]amino]benzoyl]- (9CI)

MF C20 H25 N7 O6

CI COM

Absolute stereochemistry.

L9 44 ANSWERS REGISTRY COPYRIGHT 2000 ACS

IN L-Glutamic acid, N-[4-[[(2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-1]]

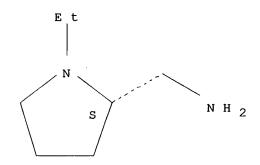
6-pteridinyl)methyl]amino]benzoyl]-, (S)-, compd. with (S)-1-ethyl-2-pyrrolidinemethanamine (1:1) (9CI)
MF C20 H25 N7 O6 . C7 H16 N2

CM 1

Absolute stereochemistry.

CM 2

Absolute stereochemistry. Rotation (-).



- L9 44 ANSWERS 'REGISTRY COPYRIGHT 2000 ACS
- IN L-Glutamic acid, N-[4-[[[(6S)-2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl]methyl]amino]benzoyl]-, calcium salt (9CI)
- MF C20 H25 N7 O6 . x Ca

🛡 х Са

L9 44 ANSWERS REGISTRY COPYRIGHT 2000 ACS

IN L-Glutamic acid, N-[4-[[2-(2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl)ethyl]amino]benzoyl]- (9CI)

MF C21 H27 N7 O6

CI COM

IN L-Glutamic acid, N-[4-[[(2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl)methyl]amino]benzoyl-1,2,3,4,5,6-13C6]-(9CI)

MF C20 H25 N7 O6

Absolute stereochemistry.

L9 44 ANSWERS REGISTRY COPYRIGHT 2000 ACS

IN L-Glutamic acid, N-[4-[[(2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-, (S)-, compd. with cyclohexanamine (9CI)

CM · 1

Absolute stereochemistry.

CM 2

L9 44 ANSWERS REGISTRY COPYRIGHT 2000 ACS

IN L-Glutamic acid, N-[4-[[(2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-, disodium salt (9CI)

MF C20 H25 N7 O6 . 2 Na

Νa

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L-Glutamic acid, N-[4-[[(2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-, barium salt (1:1) (9CI) C20 H25 N7 O6 . Ba IN

MF

Ва

L9 44 ANSWERS REGISTRY COPYRIGHT 2000 ACS

IN L-Glutamic acid, N-[4-[[(2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-, (S)-, compd. with .gamma.-cyclodextrin (1:1) (9CI)

MF C48 H80 O40 . C20 H25 N7 O6

CM 1

CM 2

IN L-Glutamic acid, N-[4-[[2-(2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl)ethyl]amino]benzoyl]-, (S)- (9CI)

MF C21 H27 N7 O6

L-Glutamic acid, N-[4-[[(2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-, barium salt (9CI) C20 H25 N7 O6 . x Ba IN

MF

IN L-Glutamic acid, N-[4-[[(2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-, calcium salt (1:1), (S)- (9CI)

MF C20 H25 N7 O6 . Ca

Absolute stereochemistry.

● Ca

L9 44 ANSWERS REGISTRY COPYRIGHT 2000 ACS

IN L-Glutamic acid, N-[4-[[(2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-, calcium salt (9CI)

MF C20 H25 N7 O6 . x Ca

🗣 х Са

L9 44 ANSWERS REGISTRY COPYRIGHT 2000 ACS

IN L-Glutamic acid, N-[4-[[(2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-, didehydro deriv. (9CI)

MF C20 H23 N7 06

CI IDS

CM 1

IN L-Glutamic acid, N-[4-[[(2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl)methyl]amino]benzoyl]- (9CI)

MF C20 H25 N7 O6

CI COM

Absolute stereochemistry.

L9 44 ANSWERS REGISTRY COPYRIGHT 2000 ACS

IN L-Glutamic acid, N-[4-[[(2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-, compd. with N-(1-methylethyl)-2-propanamine (9CI)

MF C20 H25 N7 O6 . x C6 H15 N

Absolute stereochemistry.

CM 2

L9 44 ANSWERS REGISTRY COPYRIGHT 2000 ACS

IN L-Glutamic acid, N-[4-[[(2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl)methylene]amino]benzoyl]- (9CI)

MF C20 H23 N7 O6

Absolute stereochemistry. Double bond geometry unknown.

L9 44 ANSWERS REGISTRY COPYRIGHT 2000 ACS

IN L-Glutamic acid, N-[4-[[[(6R)-2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl]methyl]amino]benzoyl]- (9CI)

MF C20 H25 N7 O6

CI COM

Absolute stereochemistry.

ALL ANSWERS HAVE BEEN SCANNED

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L10 ANSWER 1 OF 6 REGISTRY COPYRIGHT 2000 ACS

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CN L-Glutamic acid, N-[4-[[(2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-, calcium salt (1:1), (S)- (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C20 H25 N7 O6 . Ca

SR CA

LC STN Files: CA, CAPLUS, USPATFULL

CRN (31690-09-2)

Absolute stereochemistry.

• Ca

2 REFERENCES IN FILE CA (1967 TO DATE)

3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 122:109342 Method for the industrial preparation of (6S) folic acid derivatives by chromatographic separation. Ambrosini, Leonardo; Sala, Bruno (Irca S.p.A. - Industrie Ricerche Chimiche d'Albano, Italy). Eur. Pat. Appl. EP 627435 Al 19941207, 6 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1993-108752 19930601. PATENT NO. KIND DATE APPLICATION NO. DATE

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REFERENCE 2: 119:270915 Preparation of N5-methyl- and
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           diastereomers. Vecchi, Giuseppe (APR Applied Pharma Research S. A.,
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           R: AT, BE, DE, DK, ES, FR, GB, IT, NL. (English). CODEN: EPXXDW.
           APPLICATION: EP 1992-203089 19921007. PRIORITY: CH 1991-2986 19911010.
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L10 ANSWER 2 OF 6 REGISTRY COPYRIGHT 2000 ACS
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1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 116:129615 Preparation and resolution of ammonium

N5-methyl-5,6,7,8-tetrahydrofolates for use as drugs. Marazza, Fabrizio;
Jacques, Jean (Sapec S. A., Switz.). Eur. Pat. Appl. EP 455013 Al
19911106, 24 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB,
GR, IT, LI, LU, NL, SE. (German). CODEN: EPXXDW. APPLICATION: EP
1991-105715 19910411. PRIORITY: CH 1990-1255 19900412.

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L10 ANSWER 3 OF 6 REGISTRY COPYRIGHT 2000 ACS

RN 5 139418-88-5 REGISTRY

CN L-Glutamic acid, N-[4-[(2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-, calcium salt (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C20 H25 N7 O6 . x Ca

SR CA

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LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL

CRN (134-35-0)

Absolute stereochemistry.

● x Ca

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3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:326081 Compositions for the treatment and prevention of neurological and pathopsychological diseases. Buchholz, Herwig; Meduski, Jerzy D. (Merck Patent G.m.b.H., Germany). PCT Int. Appl. WO 2000025793 A1 20000511, 21 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-EP7688 19991013. PRIORITY: US 1998-PV106230 19981030.

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REFERENCE 3: 116:129615 Preparation and resolution of ammonium
    N5-methyl-5,6,7,8-tetrahydrofolates for use as drugs. Marazza, Fabrizio;
     Jacques, Jean (Sapec S. A., Switz.). Eur. Pat. Appl. EP 455013 A1
     19911106, 24 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB,
     GR, IT, LI, LU, NL, SE. (German). CODEN: EPXXDW. APPLICATION: EP
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L10 ANSWER 4 OF 6 REGISTRY COPYRIGHT 2000 ACS

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RN 129025 21-4 REGISTRY

CN L-Glutamic acid, N-[4-[[[(6S)-2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl]methyl]amino]benzoyl]-, calcium salt (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN L-Glutamic acid, N-[4-[[(2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-, calcium salt, (S)-

FS STEREOSEARCH

MF C20 H25 N7 O6 . x Ca

SR CA

LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL

CRN (31690-09-2)

Absolute stereochemistry.

• x Ca

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REFERENCE 1: 131:78463 The use of tetrahydrofolates in natural stereoisomeric form for production of a pharmaceutical preparation for influencing the homocysteine level, particularly for assisting the remethylation of homocysteine. Mueller, Hans Rudolf; Ulmann, Martin; Moser, Rudolf (Eprova A.-G., Switz.). Can. Pat. Appl. CA 2240571 AA 19981213, 14 pp. (English). CODEN: CPXXEB. APPLICATION: CA 1998-2240571

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REFERENCE 4: 116:129615 Preparation and resolution of ammonium N5-methyl-5,6,7,8-tetrahydrofolates for use as drugs. Marazza, Fabrizio; Jacques, Jean (Sapec S. A., Switz.). Eur. Pat. Appl. EP 455013 A1

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REFERENCE 5: 113:110799 Separation of 5,10-methenyl-(6R)-, 5-formyl-(6S)-,
     and 5-methyl-(6S)-tetrahydrofolate mixtures via fractional
    crystallization. Mueller, Hans Rudolf; Ulmann, Martin; Conti, Josef;
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                           19910628
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    ZA 8904896
                      Α
                           19900328
                                                           19890628
                                          CA 1989-604256
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                      Α1
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                      Α2
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                                          JP 1989-165487
                                                           19890629
    JP 08026022
                      В4
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                                          US 1989-373007
   _US 5006655 ~
                      Α
                           19910409
                                                           19890629
L10 ANSWER 5 OF 6 REGISTRY COPYRIGHT 2000 ACS
```

RN 80402-47-7 REGISTRY

CN L-Glutamic acid, N-[4-[[(2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl)methyl]methylamino]benzoyl]-, calcium salt (1:1) (9CI)

(CA INDEX NAME)

FS STEREOSEARCH

MF C21 H27 N7 O6 . Ca

LC STN Files: CA, CAPLUS, TOXLIT

CRN (1553 - 43 - 1)

Absolute stereochemistry.

Сa

1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 96:45942 Synthesis of pseudocofactor analogs as potential inhibitors of the folate enzymes. Temple, Carroll, Jr.; Bennett, L. Lee, Jr.; Rose, Jerry D.; Elliott, Robert D.; Montgomery, John H. (Kettering-Meyer Lab., Southern Res. Inst., Birmingham, AL, 35255, USA). J. Med. Chem., 25(2), 161-6 (English) 1982. CODEN: JMCMAR. ISSN: 0022-2623.

L10 ANSWER 6 OF 6 REGISTRY COPYRIGHT 2000 ACS RN 26560-38-3 REGISTRY

L-Glutamic acid, N-[4-[[(2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-CN 6-pteridinyl)methyl]amino]benzoyl]-, calcium salt (1:1) (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

Glutamic acid, N-[p-[[(2-amino-5,6,7,8-tetrahydro-4-hydroxy-5-methyl-6pteridinyl)methyl]amino]benzoyl]-, calcium salt (1:1), L- (8CI)

OTHER NAMES:

Calcium N5-methyltetrahydrofolate CN

STEREOSEARCH FS

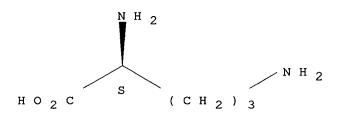
MF C20 H25 N7 O6 . Ca CRN 134-35-0 CMF C20 H25 N7 O6

Absolute stereochemistry.

CM 2

CRN 70-26-8 CMF C5 H12 N2 O2

Absolute stereochemistry.



2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 77:66198 Tetrahydrofolic acid salts for injection. Murakami, Masuo; Imai, Kazuo; Ito, Yoshiki (Yamanouchi Pharmaceutical Co., Ltd.). Japan. JP 47019917 B4 19720606 Showa, 3 pp. (Japanese). CODEN: JAXXAD. APPLICATION: JP 1970-133 19691226.

REFERENCE 2: 75:64273 Salts of 5,6,7,8-tetrahydrofolic acid with basic amino

acids. Murakami, Masuo; Imai, Kazuo; Ito, Noriki (Yamanouchi Pharmaceutical Co. Ltd.). Ger. Offen 2063027 19710701, 7 pp. (German). CODEN: GWXXBX. PRIORITY: JP 19691226. PATENT NO. KIND DATE APPLICATION NO. DATE

PI	DE 2063027	A	19710701	DE 1970-2063027	19701222
	FR 2081399	A5	19711203	FR 1970-46665	19701224

L5 ANSWER 3 OF 11 REGISTRY COPYRIGHT 2000 ACS

RN 33140-03-3 REGISTRY

CN L-Glutamic acid, N-[4-[[(2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-, compd. with L-arginine (1:2) (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Glutamic acid, N-[p-[[(2-amino-5,6,7,8-tetrahydro-4-hydroxy-5-methyl-6-pteridinyl)methyl]amino]benzoyl]-, L-, compd. with L-arginine (1:2) (8CI)

CN L-Arginine, N-[4-[[(2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-L-glutamate (2:1) (9CI)

FS STEREOSEARCH

MF C20 H25 N7 O6 . 2 C6 H14 N4 O2

LC STN Files: CA, CAPLUS

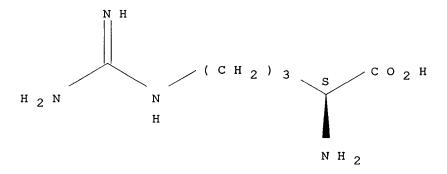
CM 1

CRN 134-35-0 CMF C20 H25 N7 O6

Absolute stereochemistry.

CM 2

CRN 74-79-3 CMF C6 H14 N4 O2



- 2 REFERENCES IN FILE CA (1967 TO DATE)
- 2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 77:66198 Tetrahydrofolic acid salts for injection. Murakami, Masuo; Imai, Kazuo; Ito, Yoshiki (Yamanouchi Pharmaceutical Co., Ltd.). Japan. JP 47019917 B4 19720606 Showa, 3 pp. (Japanese). CODEN: JAXXAD. APPLICATION: JP 1970-133 19691226.

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
[JP 47019917	В4	19720606	JP 1970-133	19691226

REFERENCE 2: 75:64273 Salts of 5,6,7,8-tetrahydrofolic acid with basic amino

acids. Murakami, Masuo; Imai, Kazuo; Ito, Noriki (Yamanouchi Pharmaceutical Co. Ltd.). Ger. Offen. DE 2063027 19710701, 7 pp. (German). CODEN: GWXXBX. PRIORITY: JP 19691226.

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 2063027	A	19710701	DE 1970-2063027	19701222
	FR 2081399	A5	19711203	FR 1970-46665	19701224

- L5 ANSWER 4 OF 11 REGISTRY COPYRIGHT 2000 ACS
- RN 31690-09-2 REGISTRY
- CN L-Glutamic acid, N-[4-[[[(6S)-2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl]methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)
 OTHER CA INDEX NAMES:
- CN Glutamic acid, N-[p-[[(2-amino-5,6,7,8-tetrahydro-4-hydroxy-5-methyl-6-pteridinyl)methyl]amino]benzoyl]-, L-(-)-(8CI)
- CN L-Glutamic acid, N-[4-[(2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-, (S)-

OTHER NAMES:

PΙ

- CN (6S)-5-Methyltetrahydrofolic acid
- CN l-N5-Methyl-L-tetrahydrofolic acid
- FS STEREOSEARCH
- DR 150950-03-1
- MF C20 H25 N7 O6
- CI COM
- LC STN Files: BEILSTEIN*, CA, CAPLUS, IPA, TOXLINE, TOXLIT, USPATFULL (*File contains numerically searchable property data)

- 43 REFERENCES IN FILE CA (1967 TO DATE)
- 3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
- 43 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:30292 Bioactivity of orally administered unnatural isomers,

[6R]-5-formyltetrahydrofolate and [6S]-5,10-methenyltetrahydrofolate, in humans. Baggott, Joseph E.; Tamura, Tsunenobu (Department of Nutrition Sciences, University of Alabama at Birmingham, Birmingham, AL, 35294-3360,

USA). Biochim. Biophys. Acta, 1472(1-2), 323-332 (English) 1999. CODEN: BBACAQ. ISSN: 0006-3002. Publisher: Elsevier Science B.V..

REFERENCE 2: 131:78463 The use of tetrahydrofolates in natural stereoisomeric form for production of a pharmaceutical preparation for influencing the homocysteine level, particularly for assisting the remethylation of homocysteine. Mueller, Hans Rudolf; Ulmann, Martin; Moser, Rudolf (Eprova A.-G., Switz.). Can. Pat. Appl. CA 2240571 AA 19981213, 14 pp. (English). CODEN: CPXXEB. APPLICATION: CA 1998-2240571

19980612. PRIORITY: CH 1997-1456 19970613.

	19900012. INTONITI. ON 1997 1430 19970013.						
	PATENT NO.	KIND DATE	APPLICATION NO.	DATE			
ΡI	CA 2240571	AA 19981213	CA 1998-2240571	19980612			
	EP 898965	A2 19990303	EP 1998-110302	19980605			
	R: AT, BE,	CH, DE, DK, ES, FR,	GB, GR, IT, LI, LU,	NL, SE, MC, PT,			
	IE, SI,	LT, LV, FI, RO					
	JP 11116482	A2 19990427	JP 1998-162405	19980610			
	AU 9870079	A1 19981217	AU 1998-70079	19980611			
	US 6011040	A 20000104	US 1998-95572	19980611			
	ZA 9805129	A 19981214	ZA 1998-5129	19980612			
	CN 1205206	A 19990120	CN 1998-102983	19980612			

REFERENCE 3: 131:69925 Complete mapping of divergent amino acids responsible

for differential ligand binding of folate receptors .alpha. and .beta.. Maziarz, Karen M.; Monaco, Hugo L.; Shen, Feng; Ratnam, Manohar

(Department of Biochemistry and Molecular Biology, Medical College of Ohio, Toledo, OH, 43614-5804, USA). J. Biol. Chem., 274(16), 11086-11091 (English) 1999. CODEN: JBCHA3. ISSN: 0021-9258. Publisher: American Society for Biochemistry and Molecular Biology.

REFERENCE 4: 126:340207 Identification of Amino Acid Residues that Determine

the Differential Ligand Specificities of Folate Receptors .alpha. and .beta.. Shen, Feng; Zheng, Xuan; Wang, Jianyong; Ratnam, Manohar (Department of Biochemistry Molecular Biology, Medical College of Ohio, Toledo, OH, 43699-0008, USA). Biochemistry, 36(20), 6157-6163 (English) 1997. CODEN: BICHAW. ISSN: 0006-2960. Publisher: American Chemical Society.

- REFERENCE 5: 124:110907 A Conformational Change in the Methyltransferase from Clostridium thermoaceticum Facilitates the Methyl Transfer from (6S)-Methyltetrahydrofolate to the Corrinoid/Iron Sulfur Protein in the Acetyl-CoA Pathway. Zhao, Shaying; Ragsdale, Stephen W. (Department of Biochemistry, University of Nebraska, Lincoln, NE, 68588-0664, USA). Biochemistry, 35(7), 2476-81 (English) 1996. CODEN: BICHAW. ISSN: 0006-2960.
- REFERENCE 6: 122:259142 Folate Receptor Type .gamma. Is Primarily a Secretory Protein Due to Lack of an Efficient Signal for Glycosylphosphatidylinositol Modification: Protein Characterization and Cell Type Specificity. Shen, Feng; Wu, Marietta; Ross, John F.; Miller, Danielle; Ratnam, Manohar (Department of Biochemistry and Molecular Biology, Medical College of Ohio, Toledo, OH, 43699-0008, USA). Biochemistry, 34(16), 5660-5 (English) 1995. CODEN: BICHAW. ISSN: 0006-2960.
- REFERENCE 7: 121:245273 Different Stereospecific Protein Binding of Tetrahydrofolates to Human Serum Albumin. Mader, Robert M.; Steger, Guenther G.; Rizovski, Blanka; Jakesz, Raimund; Rainer, Hugo (Department of Internal Medicine I, University of Vienna, Vienna, A-1090, Austria).

 J. Pharm. Sci., 83(9), 1247-9 (English) 1994. CODEN: JPMSAE. ISSN: 0022-3549.
- REFERENCE 8: 121:99010 Pharmacokinetics of rac-leucovorin vs. [S]-leucovorin

in patients with advanced gastrointestinal cancer. Mader, Robert M.; Steger, Gunther G.; Rizovski, Blanka; Sieder, Anna E.; Locker, Gottfried; Gnant, Michael F. X.; Jakesz, Raimund; Rainer, Hugo (Dep. Intern. Med. I, Univ. Vienna, Vienna, A-1090, Austria). Br. J. Clin. Pharmacol., 37(3), 243-8 (English) 1994. CODEN: BCPHBM. ISSN: 0306-5251.

REFERENCE 9: 121:35195 Process for the preparation of (6S)-5,6,7,8-tetrahydrofolic acid. Jequier, Pascal; Marazza, Fabrizio (Sapec s.a. Fine Chemicals, Switz.). Eur. Pat. Appl. EP 600460 A1 19940608, 6 pp. DESIGNATED STATES: R: CH, DE, ES, FR, GB, IT, LI. (German). CODEN: EPXXDW. APPLICATION: EP 1993-119354 19931201. PRIORITY: CH 1992-3674 19921201.

PA	rent no.	KIND	DATE	APPLICATION NO.	DATE
PI EP	600460	A1	19940608	EP 1993-119354	19931201
EP	600460	B1	19990217		
	R: CH, DE,	ES, FR	, GB, IT, LI		
CH	686672	Α	19960531	CH 1992-3674	19921201
JP	06211857	A2	19940802	JP 1993-301646	19931201
JP	2588363	B2	19970305		
US	5489684	A	19960206	US 1993-159542	19931201

REFERENCE 10: 121:365 Role of folylpolyglutamate synthetase in the metabolism

and cytotoxicity of 5-deazaacyclotetrahydrofolate, an anti-purine drug.
Kim, Jong Sang; Shane, Barry (Dep. Nutr. Sci., Univ. California,

CA, 94720, USA). J. Biol. Chem., 269(13), 9714-20 (English) 1994. CODEN:

JBCHA3. ISSN: 0021-9258.

L5 ANSWER 5 OF 11 REGISTRY COPYRIGHT 2000 ACS

RN 31690-08-1 REGISTRY

CN L-Glutamic acid, N-[4-[[(6R)-2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl]methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:

CN Glutamic acid, N-[p-[[(2-amino-5,6,7,8-tetrahydro-4-hydroxy-5-methyl-6-pteridinyl)methyl]amino]benzoyl]-, L-(+)- (8CI)

CN L-Glutamic acid, N-[4-[[(2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-, (R)-

OTHER NAMES:

CN d-N5-Methyl-L-tetrahydrofolic acid

FS STEREOSEARCH

MF C20 H25 N7 O6

CI COM

LC STN Files: BEILSTEIN*, CA, CAPLUS, TOXLIT, USPATFULL (*File contains numerically searchable property data)

Absolute stereochemistry.

23 REFERENCES IN FILE CA (1967 TO DATE)

24 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:172014 Folic acid reverts dysfunction of endothelial nitric

oxide synthase. Stroes, E. S. G.; Van Faassen, E. E.; Yo, M.; Martasek, P.; Boer, P.; Govers, R.; Rabelink, T. J. (Department of Vascular Medicine, University Hospital Utrecht, Utrecht, 3584, Neth.). Circ. Res.,

- 86(11), 1129-1134 (English) 2000. CODEN: CIRUAL. ISSN: 0009-7330. Publisher: Lippincott Williams & Wilkins.
- REFERENCE 2: 131:69925 Complete mapping of divergent amino acids responsible

for differential ligand binding of folate receptors .alpha. and .beta.. Maziarz, Karen M.; Monaco, Hugo L.; Shen, Feng; Ratnam, Manohar (Department of Biochemistry and Molecular Biology, Medical College of Ohio, Toledo, OH, 43614-5804, USA). J. Biol. Chem., 274(16), 11086-11091 (English) 1999. CODEN: JBCHA3. ISSN: 0021-9258. Publisher: American Society for Biochemistry and Molecular Biology.

- REFERENCE 3: 126:340207 Identification of Amino Acid Residues that Determine
 - the Differential Ligand Specificities of Folate Receptors .alpha. and .beta.. Shen, Feng; Zheng, Xuan; Wang, Jianyong; Ratnam, Manohar (Department of Biochemistry Molecular Biology, Medical College of Ohio, Toledo, OH, 43699-0008, USA). Biochemistry, 36(20), 6157-6163 (English) 1997. CODEN: BICHAW. ISSN: 0006-2960. Publisher: American Chemical Society.
- REFERENCE 4: 122:259142 Folate Receptor Type .gamma. Is Primarily a Secretory Protein Due to Lack of an Efficient Signal for Glycosylphosphatidylinositol Modification: Protein Characterization and Cell Type Specificity. Shen, Feng; Wu, Marietta; Ross, John F.; Miller, Danielle; Ratnam, Manohar (Department of Biochemistry and Molecular Biology, Medical College of Ohio, Toledo, OH, 43699-0008, USA). Biochemistry, 34(16), 5660-5 (English) 1995. CODEN: BICHAW. ISSN: 0006-2960.
- REFERENCE 5: 121:245273 Different Stereospecific Protein Binding of Tetrahydrofolates to Human Serum Albumin. Mader, Robert M.; Steger, Guenther G.; Rizovski, Blanka; Jakesz, Raimund; Rainer, Hugo (Department of Internal Medicine I, University of Vienna, Vienna, A-1090, Austria).

 J. Pharm. Sci., 83(9), 1247-9 (English) 1994. CODEN: JPMSAE. ISSN: 0022-3549.
- REFERENCE 6: 120:213304 Increased expression and characterization of two distinct folate binding proteins in murine erythroleukemia cells. Brigle,
 - Kevin E.; Spinella, Michael J.; Westin, Eric H.; Goldman, I. David (Dep. Med., Virginia Commonw. Univ., Richmond, VA, 23298, USA). Biochem. Pharmacol., 47(2), 337-45 (English) 1994. CODEN: BCPCA6. ISSN: 0006-2952.
- REFERENCE 7: 120:573 Medicaments for treating glycinamide ribonucleotide (GAR)-transformylase-dependent tumors. Grindley, Gerald Burr; Young, Charles William (Lilly, Eli, and Co., USA; Sloan-Kettering Institute for Cancer Research). Eur. Pat. Appl. EP 567324 A1 19931027, 12 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU,
- NL, PT, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1993-303117 19930421. PRIORITY: US 1992-872469 19920423.

•	PATENT NO.	KIND DATE	APPLICATION NO. DATE
ΡI	EP 567324	A1 19931027	EP 1993-303117 19930421
	R: AT, BE,	CH, DE, DK, ES, F	R, GB, GR, IE, IT, LI, LU, NL, PT, SE
	ZA 9302731	A 19941019	ZA 1993-2731 19930419
	AU 9337053	A1 19931028	AU 1993-37053 19930421
	AU 663369	B2 19951005	
	CA 2094687	AA 19931024	CA 1993-2094687 19930422

HU 64226 A2 19931228 HU 1993-1187 19930422 JP 07258088 A2 19951009 JP 1993-95784 19930422

REFERENCE 8: 119:216673 Simultaneous chiral separation of leucovorin and its

major metabolite 5-methyltetrahydrofolate by capillary electrophoresis using cyclodextrins as chiral selectors: estimation of the formation constant and mobility of the solute-cyclodextrin complexes. [Erratum to document cited in CA119(13):130804b]. Shibukawa, A.; Lloyd, D. K.; Wainer, I. W. (Dep. Oncol., McGill Univ., Montreal, PQ, H3G 1Y6, Can.). Chromatographia, 37(1-2), 113 (English) 1993. CODEN: CHRGB7. ISSN: 0009-5893.

REFERENCE 9: 119:130804 Simultaneous chiral separation of leucovorin and its

major metabolite 5-methyltetrahydrofolate by capillary electrophoresis using cyclodextrins as chiral selectors: estimation of the formation constant and mobility of the solute-cyclodextrin complexes. Shibukawa, A.; Lloyd, D. K.; Wainer, I. W. (Dep. Oncol., McGill Univ., Montreal, PQ, H3G 1Y6, Can.). Chromatographia, 35(7-8), 419-29 (English) 1993. CODEN: CHRGB7. ISSN: 0009-5893.

REFERENCE 10: 118:224956 Effect of folate diastereoisomers on the binding of 5-fluoro-2'-deoxyuridine-5'-monophosphate to thymidylate synthase. Van der Wilt, Clasina L.; Pinedo, Herbert M.; De Jong, Marion; Peters, Godefridus J. (Dep. Oncol., Free Univ. Hosp., Amsterdam, 1007 MB, Neth.). Biochem. Pharmacol., 45(5), 1177-9 (English) 1993. CODEN: BCPCA6. ISSN: 0006-2952.

L5 ANSWER 6 OF 11 REGISTRY COPYRIGHT 2000 ACS

RN 26560-38-3 REGISTRY

CN L-Glutamic acid, N-[4-[[(2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-, calcium salt (1:1) (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Glutamic acid, N-[p-[[(2-amino-5,6,7,8-tetrahydro-4-hydroxy-5-methyl-6-pteridinyl)methyl]amino]benzoyl]-, calcium salt (1:1), L- (8CI)

OTHER NAMES:

CN Calcium N5-methyltetrahydrofolate

FS STEREOSEARCH

MF C20 H25 N7 O6 . Ca

LC STN Files: CA, CAPLUS, CSCHEM, TOXLINE, TOXLIT, USPATFULL

CRN (134-35-0)

● Ca

- 8 REFERENCES IN FILE CA (1967 TO DATE)
- 9 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 121:18023 Process for stabilizing folates. Cerna, Jitka; Pristoupilova, Kamila; Kodicek, Milan; Spundova, Marcela (Czech.).

CS 276805 B6 19920812, 6 pp. (Czech). CODEN: CZXXA9. APPLICATION: CS 1990-2217 19900504.

REFERENCE 2: 120:288693 Process for the purification of crude alkaline earth

metal salts of N(5)-methyl-5,6,7,8-tetrahydrofolic acid and the uses of the purified salts. Attilio, Melera; Fabrizio, Marazza (SAPEC S.A. Fine Chemicals, Switz.). Eur. Pat. Appl. EP 539987 A2 19930505, 8 pp. DESIGNATED STATES: R: CH, DE, ES, FR, GB, IT, LI. (German). CODEN: EPXXDW. APPLICATION: EP 1992-118513 19921029. PRIORITY: CH 1991-3153 19911029.

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ΡI	EP 539987	A2	19930505	EP 1992-118513	19921029
	EP 539987	A 3	19930825		
	R: CH, DE,	ES, FR	, GB, IT, LI		
	CH 682665	A	19931029	CH 1991-3153	19911029

REFERENCE 3: 119:270915 Preparation of N5-methyl- and -formylterahydrofolate

PI

diastereomers. Vecchi, Giuseppe (APR Applied Pharma Research S. A., Switz.). Eur. Pat. Appl. EP 537842 A2 19930421, 5 pp. DESIGNATED

R: AT, BE, DE, DK, ES, FR, GB, IT, NL. (English). CODEN: EPXXDW. APPLICATION: EP 1992-203089 19921007. PRIORITY: CH 1991-2986 19911010. APPLICATION NO. DATE

PATENT NO. KIND DATE ---------EP 537842 A2 19930421 EP 537842 A3 19930505 EP 1992-203089 19921007

PΤ

R: AT, BE, DE, DK, ES, FR, GB, IT, NL

CH 683261 A 19940215 CH 1991-2986 US 5350850 A 19940927 US 1992-957176 CA 2080178 AA 19930411 CA 1992-2080179 CH 1991-2986 19911010 US 1992-957176 19921007 CA 1992-2080178 19921008

REFERENCE 4: 107:228572 Effects of 5-methyltetrahydrofolate on the activity of fluoropyrimidines against human leukemia (CCRF-CEM) cells. Mini, Enrico; Mazzei, Teresita; Coronnello, Marcella; Criscuoli, Luciana; Gualtieri, Monica; Periti, Piero; Bertino, Joseph R. (Dip. Farmacol. Preclin. Clin., Univ. Firenze, Florence, 50134, Italy). Biochem. Pharmacol., 36(18), 2905-11 (English) 1987. CODEN: BCPCA6. ISSN: 0006-2952.

REFERENCE 5: 106:50632 Alkaline earth metal salts of 5-methyltetrahydrofolic

acid. Conti, Josef; Mueller, Hans Rudolf (Eprova A.-G., Switz.). Patentschrift (Switz.) CH 649550 A 19850531, 4 pp. (German). CODEN: SWXXAS. APPLICATION: CH 1984-606 19840209.

KIND DATE APPLICATION NO. DATE PATENT NO. KIND DATE ______ _____ CH 649550 A 19850531 CH 1984-606 19840209

- REFERENCE 6: 99:205503 Pharmacokinetics of 5-methyltetrahydrofolate in normal adults. Periti, P.; Ciuffi, M.; Coronnello, M.; Mazzei, T.; Mini, E. (Inst. Pharmacol. Toxicol., Univ. Florence, Florence, Italy). Chemioterapia, 2(2), 83-7 (English) 1983. CODEN: CHEMEV.
- REFERENCE 7: 95:98320 Process for the preparation of dl-5methyltetrahydrofolic acid. Gennari, Federico (Bioresearch S.a.S., Italy). Brit. GB 1572138 19800723, 6 pp. Division of Brit. 1,572,137. (English). CODEN: BRXXAA. APPLICATION: GB 1978-12374 19770222. PATENT NO. KIND DATE APPLICATION NO. DATE _____ _____ ---------19800723 GB 1978-12374 19770222 ΡI GB 1572138 A
- REFERENCE 8: 72:111795 Convenient method for the preparation of (+1-)-5-methyltetrahydrofolic acid ((+1-)-5-methyl-5,6,7,8tetrahydropteroyl-L-monoglutamic acid). Blair, J. A.; Saunders, K. J. (Dep. Chem., Univ. Aston, Birmingham, Engl.). Anal. Biochem., 34(2), 376-81 (English) 1970. CODEN: ANBCA2.
- ANSWER 7 OF 11 REGISTRY COPYRIGHT 2000 ACS T.5
- RN 25630-71-1 REGISTRY
- CN L-Glutamic acid, N-[4-[[2-amino-1,4,5,6,7,8-hexahydro-5-(methyl-14C)-4-oxo-6-pteridinyl]methyl]amino]benzoyl]- (9CI) (CA INDEX NAME) OTHER CA INDEX NAMES:
- Glutamic acid, N-[p-[[(2-amino-5,6,7,8-tetrahydro-4-hydroxy-5-methyl-14C-6-pteridinyl)methyl]amino]benzoyl]-, L- (8CI)
- 5-Methyl-14C-tetrahydrofolic acid
- STEREOSEARCH FS
- C20 H25 N7 O6

LC STN Files: BEILSTEIN*, CA, CAPLUS, TOXLIT

(*File contains numerically searchable property data)

Absolute stereochemistry.

2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 93:109732 Enzymic preparations of radiolabeled +-L-5-methyltetrahydrofolate and +-L-formyltetrahydrofolate. Nixon, P. F.; Bertino, J. R. (Dep. Biochem., Univ. Queensland, St. Lucia, 4067, Australia). Methods Enzymol., 66(Vitam. Coenzymes, Pt. E), 547-53 (English) 1980. CODEN: MENZAU. ISSN: 0076-6879.

REFERENCE 2: 75:58966 Enzymic preparations of radiolabeled (+)-L-5-methyltetrahydrofolate and (+)-L-5-formyltetrahydrofolate. Nixon,

P. F.; Bertino, J. R. (Sch. Med., Yale Univ., New Haven, Conn., USA). Anal. Biochem., 43(1), 162-72 (English) 1971. CODEN: ANBCA2.

L5 ANSWER 8 OF 11 REGISTRY COPYRIGHT 2000 ACS

RN 15997-98-5 REGISTRY

CN L-Glutamic acid, N-[4-[[(2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-, barium salt (1:1) (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Glutamic acid, N-[p-[[(2-amino-5,6,7,8-tetrahydro-4-hydroxy-5-methyl-6-pteridinyl)methyl]amino]benzoyl]-, barium salt (1:1), L- (8CI)

FS STEREOSEARCH

DR 20392-92-1, 26560-37-2

MF C20 H25 N7 O6 . Ba

LC STN Files: CA, CAPLUS

CRN (134-35-0)

Вa

3 REFERENCES IN FILE CA (1967 TO DATE) 3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 106:50632 Alkaline earth metal salts of 5-methyltetrahydrofolic

acid. Conti, Josef; Mueller, Hans Rudolf (Eprova A.-G., Switz.). Patentschrift (Switz.) CH 649550 A 19850531, 4 pp. (German). CODEN: SWXXAS. APPLICATION: CH 1984-606 19840209.

PATENT NO.

KIND DATE

APPLICATION NO. DATE

_____ PΙ CH 649550

19850531 Α

CH 1984-606

19840209

REFERENCE 2: 95:98320 Process for the preparation of dl-5methyltetrahydrofolic acid. Gennari, Federico (Bioresearch S.a.S., Italy). Brit. GB 1572138 19800723, 6 pp. Division of Brit. 1,572,137. (English). CODEN: BRXXAA. APPLICATION: GB 1978-12374 19770222. PATENT NO. KIND DATE APPLICATION NO. DATE

PIGB 1572138

19800723 Α

GB 1978-12374

19770222

- REFERENCE 3: 84:101195 On the mode of formation of tetrahydro-.beta.carbolines. Rommelspacher, Hans; Coper, Helmut; Strauss, Sabine (Inst. Neuropsychopharmacol., Free Univ. Berlin, Berlin, Ger.). Life Sci., 18(1), 81-8 (English) 1976. CODEN: LIFSAK.
- ANSWER 9 OF 11 REGISTRY COPYRIGHT 2000 ACS L5
- RN 7611-41-8 REGISTRY
- Glutamic acid, N-[p-[[(2-amino-5,6,7,8-tetrahydro-4-hydroxy-5-methyl-CN 6-pteridiny1-7-t)methy1]amino]benzoy1]- (7CI, 8CI) (CA INDEX NAME)
- STEREOSEARCH FS

MF C20 H24 N7 O6 T LC STN Files: CAOLD

Absolute stereochemistry.

1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L5 ANSWER 10 OF 11 REGISTRY COPYRIGHT 2000 ACS

RN 7611-40-7 REGISTRY

CN Glutamic acid, N-[p-[[(2-amino-5,6,7,8-tetrahydro-6-t-4-hydroxy-5-methyl-6-pteridinyl)methyl]amino]benzoyl]- (7CI, 8CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C20 H24 N7 O6 T

LC STN Files: CAOLD

1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

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L5 ANSWER 11 OF 11 REGISTRY COPYRIGHT 2000 ACS
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RN 134-35-0 REGISTRY

CN L-Glutamic acid, N-[4-[[(2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl)methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:

CN Glutamic acid, N-[p-[[(2-amino-5,6,7,8-tetrahydro-4-hydroxy-5-methyl-6-pteridinyl)methyl]amino]benzoyl]- (6CI)

CN Glutamic acid, N-[p-[[(2-amino-5,6,7,8-tetrahydro-4-hydroxy-5-methyl-6-pteridinyl)methyl]amino]benzoyl]-, L- (8CI)

OTHER NAMES:

CN 5-Methyl-5,6,7,8-tetrahydrofolic acid

CN 5-Methyl-5,6,7,8-tetrahydropteroyl-L-glutamic acid

CN 5-Methyltetrahydrofolic acid

CN 5-Methyltetrahydropteroyl monoglutamate

CN 5-Methyltetrahydropteroylglutamic acid

CN N-Methyltetrahydrofolate

CN N-Methyltetrahydrofolic acid

CN N5-Methyltetrahydrofolate

CN N5-Methyltetrahydrofolic acid

CN N5-Methyltetrahydropteroylglutamate

CN Prefolic A

FS STEREOSEARCH

DR 3922-58-5, 76937-22-9

MF C20 H25 N7 O6

CI COM

LC STN Files: AGRICOLA, AIDSLINE, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS,

BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CIN, DDFU, DRUGU, EMBASE, IPA, MEDLINE, NIOSHTIC, PROMT, TOXLINE, TOXLIT, USPATFULL, VETU (*File contains numerically searchable property data)

961 REFERENCES IN FILE CA (1967 TO DATE)

18 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

963 REFERENCES IN FILE CAPLUS (1967 TO DATE)

16 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 133:278144 High-performance liquid chromatographic assay for the determination of 5-methyltetrahydrofolate in human plasma. Chladek, J.; Sispera, L.; Martinkova, J. (Simkova 870, Faculty of Medicine, Department of Pharmacology, Charles University, Hradec Kralove, Czech Rep.). J. Chromatogr., B: Biomed. Sci. Appl., 744(2), 307-313 (English) 2000. CODEN: JCBBEP. ISSN: 0378-4347. Publisher: Elsevier Science B.V..

REFERENCE 2: 133:264354 Contrasting effects of oncogene expression on two carrier-mediated systems internalizing folate compounds in fisher rat 3T3 cells. Kuhnel, Jean-Marc; Chiao, Judy H.; Sirotnak, F. M. (Program of Molecular Pharmacology and Experimental Therapeutics, Memorial Sloan-Kettering Cancer Center, New York, NY, 10021, USA). J. Cell. Physiol., 184(3), 364-372 (English) 2000. CODEN: JCLLAX. ISSN: 0021-9541. Publisher: Wiley-Liss, Inc..

REFERENCE 3: 133:256805 Combinations of fibrates with B vitamins for reduction of homocysteine levels. Dierkes, Jutta; Luley, Claus; Westphal,

Sabine (Dierkes, Jutta,, Germany; Luley, Claus, Prof.Dr.; Westphal, Sabine,). Ger. Offen. DE 19910682 Al 20000921, 4 pp. (German). CODEN: GWXXBX. APPLICATION: DE 1999-19910682 19990310.

PATENT NO. KIND DATE APPLICATION NO. DATE

PI DE 19910682 A1 20000921 DE 1999-19910682 19990310

REFERENCE 4: 133:202550 Impact of the simultaneous administration of the (+)- and (-)-forms of formyl-tetrahydrofolic acid on plasma and intracellular pharmacokinetics of (-)-tetrahydrofolic acid. Schleyer, Eberhard; Rudolph, Karl Lenhard; Braess, Jan; Unterhalt, Michael; Ehninger, Gerhard; Hiddemann, Wolfgang; Kern, Wolfgang (Department of Internal Medicine I, Carl-Gustav-Carus-University, Dresden, Germany). Cancer Chemother. Pharmacol., 45(2), 165-171 (English) 2000. CODEN: CCPHDZ. ISSN: 0344-5704. Publisher: Springer-Verlag.

REFERENCE 5: 133:175691 Altered foliate metabolism and disposition in mothers

affected by a spina bifida pregnancy: influence of 677 c.fwdarw.t methylenetetrahydrofolate reductase and 2756 a.fwdarw.g methionine synthase genotypes. Lucock, Mark; Daskalakis, Ioannis; Briggs, David; Yates, Zoe; Levene, Malcolm (Research School of Medicine, Centre for Production, Growth and Development, Division of Paediatrics and Child Health, University of Leeds, Leeds General Infirmary, Leeds, West Yorkshire, LS2 9NS, UK). Mol. Genet. Metab., 70(1), 27-44 (English) 2000.

CODEN: MGMEFF. ISSN: 1096-7192. Publisher: Academic Press.

- REFERENCE 6: 133:174116 Analysis of folate form distribution by affinity followed by reversed-phase chromatography with electrochemical detection. Bagley, Pamela J.; Selhub, Jacob (Vitamin Metabolism Laboratory, Jean Mayer Human Nutrition Research Center on Aging at Tufts University, US Department of Agriculture, Boston, MA, 02111, USA). Clin. Chem. (Washington, D. C.), 46(3), 404-411 (English) 2000. CODEN: CLCHAU. ISSN:
- 0009-9147. Publisher: American Association for Clinical Chemistry.
- REFERENCE 7: 133:172014 Folic acid reverts dysfunction of endothelial nitric

oxide synthase. Stroes, E. S. G.; Van Faassen, E. E.; Yo, M.; Martasek, P.; Boer, P.; Govers, R.; Rabelink, T. J. (Department of Vascular Medicine, University Hospital Utrecht, Utrecht, 3584, Neth.). Circ.

- 86(11), 1129-1134 (English) 2000. CODEN: CIRUAL. ISSN: 0009-7330. Publisher: Lippincott Williams & Wilkins.
- REFERENCE 8: 133:146068 Trichloroethylene induced vitamin B12 and folate deficiency leads to increased formic acid excretion in the rat. Dow, J. L.; Green, T. (Zeneca, Central Toxicology Laboratory, Macclesfield, Cheshire, UK). Toxicology, 146(2-3), 123-136 (English) 2000. CODEN: TXCYAC. ISSN: 0300-483X. Publisher: Elsevier Science Ireland Ltd..
- REFERENCE 9: 133:115062 Trans-stimulation effects of folic acid derivatives on methotrexate transport by rat renal organic anion transporter, OAT-K1. Takeuchi, Ayako; Masuda, Satohiro; Saito, Hideyuki; Hashimoto, Yukiya; Inui, Ken-Ichi (Department of Pharmacy, Kyoto University Hospital,
 - of Medicine, Kyoto University, Kyoto, Japan). J. Pharmacol. Exp. Ther., 293(3), 1034-1039 (English) 2000. CODEN: JPETAB. ISSN: 0022-3565. Publisher: American Society for Pharmacology and Experimental Therapeutics.
- REFERENCE 10: 133:99302 Controlled comparison of L-5-methyltetrahydrofolate versus folic acid for the treatment of hyperhomocysteinemia in hemodialysis patients. Bostom, Andrew G.; Shemin, Douglas; Bagley, Pamela; Massy, Ziad A.; Zanabli, Abdul; Christopher, Kenneth; Spiegel, Paul; Jacques, Paul F.; Dworkin, Lance; Selhub, Jacob (Division of General

Internal Medicine, Memorial Hospital of Rhode Island, Pawtucket, RI, 02860, USA). Circulation, 101(24), 2829-2832 (English) 2000. CODEN: CIRCAZ. ISSN: 0009-7322. Publisher: Lippincott Williams & Wilkins.

EP 539987 A3 19930825 R: CH, DE, ES, FR, GB, IT, LI

CH 682665 A 19931029 CH 1991-3153 19911029

REFERENCE 3: 119:270915 Preparation of N5-methyl- and -formylterahydrofolate

R: AT, BE, DE, DK, ES, FR, GB, IT, NL. (English). CODEN: EPXXDW. APPLICATION: EP 1992-203089 19921007. PRIORITY: CH 1991-2986 19911010.

PATENT NO. KIND DATE APPLICATION NO. DATE

----PI EP 537842 A2 19930421 EP 1992-203089 19921007
EP 537842 A3 19930505
R: AT, BE, DE, DK, ES, FR, GB, IT, NL

CH 683261 A 19940215 CH 1991-2986 19911010
US 5850850 A 19940927 US 1992-957176 19921007
CA 2080178 AA 19930411 CA 1992-2080178 19921008

REFERENCE 4: 107:228572 Effects of 5-methyltetrahydrofolate on the activity of fluoropyrimidines against human leukemia (CCRF-CEM) cells. Mini, Enrico; Mazzei, Teresita; Coronnello, Marcella; Criscuoli, Luciana; Gualtieri, Monica; Periti, Piero; Bertino, Joseph R. (Dip. Farmacol. Preclin. Clin., Univ. Firenze, Florence, 50134, Italy). Biochem. Pharmacol., 36(18), 2905-11 (English) 1987. CODEN: BCPCA6. ISSN: 0006-2952.

REFERENCE 5: 106:50632 Alkaline earth metal salts of 5-methyltetrahydrofolic

acid. Conti, Josef; Mueller, Hans Rudolf (Eprova A.-G., Switz.). Patentschrift (Switz.) CH 649550 A 19850531, 4 pp. (German). CODEN: SWXXAS. APPLICATION: CH 1984-606 19840209.

PATENT NO. KIND DATE APPLICATION NO. DATE
PI CH#649550 A 19850531 CH 1984-606 19840209

- REFERENCE 6: 99:205503 Pharmacokinetics of 5-methyltetrahydrofolate in normal adults. Periti, P.; Ciuffi, M.; Coronnello, M.; Mazzei, T.; Mini, E. (Inst. Pharmacol. Toxicol., Univ. Florence, Florence, Italy). Chemioterapia, 2(2), 83-7 (English) 1983. CODEN: CHEMEV.
- REFERENCE 8: 72:111795 Convenient method for the preparation of (+1-)-5-methyltetrahydrofolic acid ((+1-)-5-methyl-5,6,7,8-tetrahydropteroyl-L-monoglutamic acid). Blair, J. A.; Saunders, K. J. (Dep. Chem., Univ. Aston, Birmingham, Engl.). Anal. Biochem., 34(2), 376-81 (English) 1970. CODEN: ANBCA2.

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RN 34418-06-9 REGISTRY

CN Glutamic acid, N-[p-[[(2-amino-5,6,7,8-tetrahydro-4-hydroxy-5-methyl-6-pteridinyl)methyl-t]amino]benzoyl-2,6-t2]-, L- (8CI) (CA INDEX NAME)

OTHER NAMES:

CN 5-Methyltetrahydrofolic acid-9,3',5'-3H

FS STEREOSEARCH

MF C20 H22 N7 O6 T3

LC STN Files: CA, CAPLUS

Absolute stereochemistry.

- 1 REFERENCES IN FILE CA (1967 TO DATE)
- 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 75:58966 Enzymic preparations of radiolabeled (+)-L-5-methyltetrahydrofolate and (+)-L-5-formyltetrahydrofolate. Nixon,

P. F.; Bertino, J. R. (Sch. Med., Yale Univ., New Haven, Conn., USA). Anal. Biochem., 43(1), 162-72 (English) 1971. CODEN: ANBCA2.

L5 ANSWER 2 OF 11 REGISTRY COPYRIGHT 2000 ACS

RN 33140-04-4 REGISTRY

CN L-Glutamic acid, N-[4-[[(2-amino-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-, compd. with L-ornithine (1:2) (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Glutamic acid, N-[p-[[(2-amino-5,6,7,8-tetrahydro-4-hydroxy-5-methyl-6-pteridinyl)methyl]amino]benzoyl]-, L-, compd. with L-ornithine (1:2) (8CI)

CN L-Ornithine, N-[4-[[(2-amino-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-L-glutamate (2:1) (9CI)

FS STEREOSEARCH

MF C20 H25 N7 O6 . 2 C5 H12 N2 O2

LC STN Files: CA, CAPLUS

CM 1

LC STN Files: CA, CAPLUS, CSCHEM, TOXLINE, TOXLIT, USPATFULL CRN (134-35-0)

Absolute stereochemistry.

● Ca

- 8 REFERENCES IN FILE CA (1967 TO DATE)
- 9 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 121:18023 Process for stabilizing folates. Cerna, Jitka; Pristoupilova, Kamila; Kodicek, Milan; Spundova, Marcela (Czech.). Czech.

CS 276805 B6 19920812, 6 pp. (Czech). CODEN: CZXXA9. APPLICATION: CS 1990-2217 19900504.

REFERENCE 2: 120:288693 Process for the purification of crude alkaline earth

metal salts of N(5)-methyl-5,6,7,8-tetrahydrofolic acid and the uses of the purified salts. Attilio, Melera; Fabrizio, Marazza (SAPEC S.A. Fine Chemicals, Switz.). Eur. Pat. Appl. EP 539987 A2 19930505, 8 pp. DESIGNATED STATES: R: CH, DE, ES, FR, GB, IT, LI. (German). CODEN: EPXXDW. APPLICATION: EP 1992-118513 19921029. PRIORITY: CH 1991-3153 19911029.